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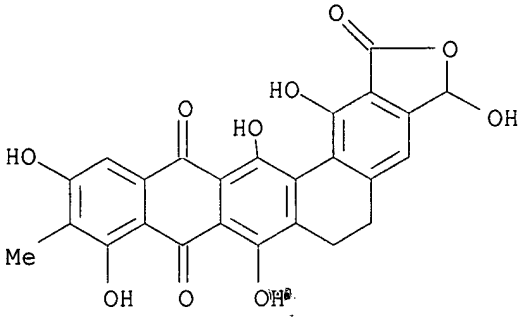
**WO 99/40908** (art.158 de la CBE).

L2  ANSWER 5 OF 473  REGISTRY  COPYRIGHT 2001 ACS
RN  300578-79-4  REGISTRY
CN  Naphtho[2',3':6,7]phenanthro[2,3-c]furan-1,8,13(3H)-trione,
    5,6-dihydro-3,7,9,11,14,15-hexahydroxy-10-methyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN  **Desmethylmadurahydroxylactone**
MF  C25 H16 O10
SR  CA
LC  STN Files:  CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s madurahydroxylactone

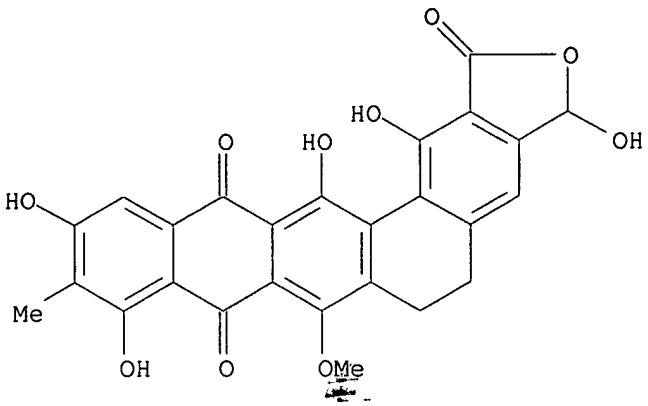
L3  2 MADURAHYDROXYLACTONE

=> s madurahydroxylactone/cn

L4  1 MADURAHYDROXYLACTONE/CN

=> d

L4  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN  160324-72-1  REGISTRY
CN  Naphtho[2',3':6,7]phenanthro[2,3-c]furan-1,8,13(3H)-trione,
    5,6-dihydro-3,9,11,14,15-pentahydroxy-7-methoxy-10-methyl- (9CI)  (CA
    INDEX NAME)
OTHER CA INDEX NAMES:
CN  Naphtho[2',3':6,7]phenanthro[2,3-c]furan-1,8,13(3H)-trione,
    5,6-dihydro-3,9,11,14,15-pentahydroxy-7-methoxy-10-methyl-, (.+-.)-
OTHER NAMES:
CN  **Madurahydroxylactone**
MF  C26 H18 O10
CI  COM
SR  CA
LC  STN Files:  CA, CAPLUS, CASREACT, USPATFULL



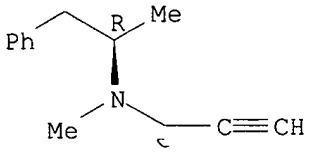

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L5 ANSWER 8 OF 8 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI **Antiviral** activity of norakin (triperiden) and related anticholainergic antiparkinsonism drugs.
SO Acta Virologica, (1984) 28/6 (501-507).
CODEN: AVIRA2
AB In view of the coincidence of **antiviral** and antiparkinsonism activities of amantadine, four antiparkinsonism drugs Norakin (triperiden), Parkopan (trihexyphenidyl), Antiparkin (diethylbenzhydramine) and Akineton (biperiden) were tested for **antiviral** activity in various virus-cell systems. Norakin inhibited the replication of influenza A viruses in chick embryo fibroblast, MDCK and Ehrlich. . .
CT Medical Descriptors:
*2 benzhydryloxy n,n diethylethylamine
*drug efficacy
*influenza virus
*influenza virus a
*measles virus
*structure activity relation
cell culture
virus replication
priority journal
in vitro study
nonhuman
chicken
*amantadine
***antivirus agent**
*biperiden
*rimantadine
*trihexyphenidyl
*triperidene
**selegiline**
RN (amantadine) 665-66-7, 768-94-5; (biperiden) 1235-82-1, 514-65-8; (rimantadine) 13392-28-4, 1501-84-4; (trihexyphenidyl) 144-11-6, 52-49-3; (triperidene) 14617-17-5; (**selegiline**) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6
AN 85025401 EMBASE
DN 1985025401
TI **Antiviral** activity of norakin (triperiden) and related anticholainergic antiparkinsonism drugs.
AU Presber H.W.; Schroeder C.; Hegenscheid B.; et al.
CS Chair of Virology, Humboldt University, 1040 Berlin, Germany
SO Acta Virologica, (1984) 28/6 (501-507).
CODEN: AVIRA2
CY Czechoslovakia
DT Journal
FS 037 Drug Literature Index
047 Virology
030 Pharmacology
LA English

L2 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2000 ACS
RN 14611-51-9 REGISTRY
CN Benzeneethanamine, N,.alpha.-dimethyl-N-2-propynyl-, (.alpha.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, N,.alpha.-dimethyl-N-2-propynyl-, (R)-
CN Phenethylamine, N,.alpha.-dimethyl-N-2-propynyl-, L-(-)- (8CI)
OTHER NAMES:
CN (-)-Deprenil
CN **(-)-Deprenyl**
CN (-)-Selegiline
CN **(R)-(-)-Deprenyl**
CN Jumex
CN **L-Deprenyl**
CN **l-Deprenyl**
CN Selegiline
FS STEREOSEARCH
DR 172964-89-5
MF C13 H17 N
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, PHAR, PROMT, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (-).

desmethyl = w/o one methyl group




742 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
743 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
AN 1998:585951 CAPLUS
DN 129:184245
TI Application of aminergic agents in medications for treatment of viral infections of the central nervous system
IN Ter Meulen, Volker; Riederer, Peter; Czub, Markus; Gerlach, Manfred
PA Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 19708461 | A1 | 19980827 | DE 1997-19708461 | 19970218 <-- |

=> d ab

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
AB Viral (esp. retroviral) infections of the central nervous system are treated with an aminergic agent at a dose such as to establish a drug concn. in the target cells below that which affects viral gene expression.
Suitable aminergic agents include dopaminergic agonists and antagonists, MAO-B inhibitors, D-methylselegiline, adamantine, and psychotropic and neuroleptic agents. Thus, in neonatal rats infected with murine leukemia virus (a microgliatropic retrovirus), development of spongiform encephalopathy was inhibited by i.p. injection of selegiline (0.05 mg/kg on days 15, 22, and 30 after infection).

=>

L11 ANSWER 6 OF 7 USPATFULL
SUMM . . . fluconazole, ritonavir, itraconazole, miconazole, erythromycin and troleandomycin have been identified as inhibitors of the first-pass effect. These compounds, however, are **antiviral**, antimicrobial, or antifungal agents. Because of the heightened current awareness of the fact that overuse of such agents can result in resistant microbial strains, because some of the most effective inhibitors are antimicrobials, and because transplant and **HIV** -infected patients have compromised immune systems, the use of these inhibitors of the first-pass effect has significant drawbacks and, for example,. . .
DETD . . . or less, more preferably 50% or less. Examples include, in addition to those incorporated by reference above, ritonavir, saquinavir, indinavir, L-**deprenyl**, tacrolimus, cyclosporin A (Sandimmune.RTM.), cyclosporin A (Neoral.RTM.), nelfinavir, VX-478/141W94, felodipine, nifedipine and sumatriptan. Such co-formulations include the invention citrus-derived substance. . .
AN 1999:151257 USPATFULL
TI Anti-first-pass effect compounds and citrus extract
IN Harris, James W., Cocoa Beach, FL, United States
PA Bioavailability Systems, L.L.C., Cocoa Beach, FL, United States (U.S. corporation)
PI US 5990154 19991123
AI US 1998-82939 19980522 (9)
PRAI US 1997-48183 19970530 (60)
DT Utility
EXNAM Primary Examiner: Ramsuer, Robert W.; Assistant Examiner: Solola, Taofiq
A
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 894
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 7 OF 7 USPATFULL
DETD . . . invention include analgesics, anesthetics, antifungals, antibiotics, antiinflammatories, anthelmintics, antidotes, antiemetics, antihistamines, antihypertensives, antimalarials, antimicrobials, antipsychotics, antipyretics, antiseptics, antiarthritics, antituberculotics, antitussives, **antivirals**, cardioactive drugs, cathartics, chemotherapeutic agents, corticoids (steroids), antidepressants, depressants, diagnostic aids, diuretics, enzymes, expectorants, hormones, hypnotics, minerals, nutritional supplements, parasympathomimetics,. . .
DETD . . . in the treatment of renal cell carcinoma, hairy cell leukemia, Kaposi's sarcoma, melanoma, and T-cell lymphoma, as well as an **antiviral** agent in the treatment of non-A,B-hepatitis, genital warts, Epstein-Barr virus, CMV, AIDS, and rhinovirus.
DETD . . . red blood cells; the interleukins; interferon-gamma, a cytokine protein produced by vertebrate cells following a virus infection and possessing potent **antiviral** effects; Vasotec.RTM., a antihypertensive (Enalapril maleate, Merck, Sharp & Dohme, West Point, Pa.) Capoten.RTM., a antihypertensive (Captopril, E. R. Squibb. . .
DETD . . . sequences of double-stranded DNA and are intended to inhibit selectively the transcription of disease-causing genes, such as viral genes, e.g., **HIV** and herpes simplex virus, and oncogenes, i.e., they stop protein production at the cell nucleus. These drugs bind

directly to. . .
DETD . . . be utilized with a variety of pharmaceutical agents having tertiary amine groups. In a preferred embodiment, the pharmaceutical agent comprises **deprenyl**, as illustrated below: ##STR1##
DETD . . . apart from its carrier function. An example of a therapeutic chemical modifier is oligomeric or polymeric lysine (polylysine). Polylysine possesses **antiviral** and antibacterial activities, as well as a specific affinity for tumor cells in cancerous tissue. Ryser, H. J.-P. and Shen,. . .
DETD 5.3 Preparation of **deprenyl**-N-(morpholine-N-carbonyloxymethyl), iodide salt
DETD To a solution of **deprenyl** hydrochloride (146 mg, 0.654 mmol) in acetonitrile (10 ml) was added the iodo carbamate prepared above (180 mg, 0.654 mmol).. . .
DETD 6.19 Preparation of **deprenyl**-N-ethoxycarbonyloxymethyl, iodide salt
DETD To a solution of **deprenyl** (424 mg, 2.3 mmol) in acetonitrile (5 ml) was added chloromethyl ethyl carbonate (315 mg, 2.3 mmol) and sodium iodide. . .
DETD 6.20 Preparation of **deprenyl**-N-octyloxycarbonyloxymethyl, iodide salt
DETD To a solution of **deprenyl** (170 mg, 0.91 mmol) in acetonitrile (5 ml) was added iodomethyl octyl carbonate (290 mg, 0.91 mmol). The reaction mixture. . .
DETD 6.21 Preparation of **deprenyl**-N-butyroyloxymethyl, iodide salt
DETD To a solution of **deprenyl** (139 mg, 0.743 mmol) in acetonitrile (5 ml) was added iodomethyl butyrate (169 mg, 0.743 mmol). The reaction mixture was. . .
DETD 6.22 Preparation of **deprenyl**-N-pivaloyloxymethyl, iodide salt
DETD To a solution of **deprenyl** (240 mg, 1.28 mmol) in acetonitrile (5 ml) was added chloromethyl 2,2-dimethylpropionate (193 mg, 1.28 mmol) and sodium iodide (192. . .
DETD 6.23 Preparation of **deprenyl**-N-acetoxymethyl, bromide salt
DETD To a solution of **deprenyl** (100 mg, 0.654 mmol) in acetonitrile (5 ml) was added bromomethyl acetate (146 mg, 0.654 mmol). The reaction mixture was. . .
DETD To a solution of **deprenyl** (424 mg, 2.3 mmol) in acetonitrile (5 ml) was added chloromethyl ethyl carbonate (315 mg, 2.3 mmol), followed by sodium. . .
DETD . . . 1 hr
carboxamide), chloride salt
cisapride-N-(6-trimethylammoniohexanoyl-oxymethylammonio), diiodide salt
1 hr
cisapride-N-acetoxymethylammonio, iodide salt
6.5 min
cisapride-N-butyroyloxymethylammonio,
7.6 min
iodide salt
cisapride-N-ethyoxycarbonyloxymethylammonio,
4.4 min
iodide salt
cisapride-N-lauroyloxymethylammonio,
5.4 min
iodide salt
**deprenyl**-N-acetoxymethyl, bromide salt
4.2 min
**deprenyl**-N-benzoyloxymethyl, iodide salt
5 min
**deprenyl**-N-butyroyloxy-1-ethyl, bromide salt
28 min
**deprenyl**-N-butyroyloxymethyl, iodide salt
17 sec
**deprenyl**-N-ethoxycarbonyloxymethyl,

71 sec
iodide salt
**deprenyl**-N-octyloxycarbonyloxymethyl,
26 sec
iodide salt
**deprenyl**-N-pivaloyloxymethyl, iodide salt
20 min
methotrexate-bis-(4-trimethylammoniobutyroyl-
1.8 hr
oxymethyl ester), diiodide salt
morphine-6-O-(trimethylammoniobutyrate
26 hr
chloride, hydrochloride salt
progesterone-3-(4-N,N,N-trimethylammonio-
3 hr
butyrate enol ester, bromide salt
progesterone-3-betainoyl enol. . .

AN 97:17918 USPATFULL
TI Compositions and methods for enhanced drug delivery
IN Hale, Ron L., Woodside, CA, United States
Lu, Amy, Los Altos, CA, United States
Solas, Dennis, San Francisco, CA, United States
Selick, Harold E., Belmont, CA, United States
Oldenburg, Kevin R., Fremont, CA, United States
Zaffaroni, Alejandro C., Atherton, CA, United States
PA Affymax Technologies N.V., Middlesex, England (non-U.S. corporation)
PI US 5607691 19970304
AI US 1995-449188 19950524 (8)
RLI Continuation of Ser. No. US 1993-164293, filed on 9 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-77296, filed on 14 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-898219, filed on 12 Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 1993-9463, filed on 27 Jan 1993, now
abandoned
DT Utility
EXNAM Primary Examiner: Levy, Neil S.
LREP Stevens, Lauren L.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5349
CAS INDEXING IS AVAILABLE FOR THIS PATENT.